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### **REMARKS**

Claims 60-117 are currently pending and presented for examination. Claims 1-59 are canceled. Applicants reserve their right to pursue the subject matter of any or all of the canceled claims in one or more continuing applications.

Claims 60, 64, 65, 69, 71, 75, 76, 80, 83, 87, 88 and 92 are currently amended. In particular, independent claims 60, 71 and 83 are amended to no longer recite "a non-permanent sealant." Claims 64, 75 and 87 are amended to recite that "said first assay location and said second assay location are separated by a gasket." Claims 65, 76 and 88 are amended to recite that "said gasket comprises rubber or silicon." Support for each of these amendments can be found at page 10, lines 1-24 and elsewhere throughout the specification. Accordingly, no new matter is added by way of these amendments.

Claims 94-117 are new. Support for new independent claim 94 can be found in the claims and specification as originally filed, for example, at page 3, lines 3-8; page 12, line 34 to page 13, line 18; page 27, lines 20-22; page 29, lines 25-27 and page 30, lines 19-23. Support for dependent claims 95 and 96 can be found at page 27, lines 20-32 and elsewhere throughout the specification. Support for dependent claim 97 can be found at page 13, lines 1-9, at page 38, lines 14-21 and elsewhere throughout the specification. Support for dependent claim 98 can be found at page 8, lines 1-6 and elsewhere throughout the specification. Support for dependent claim 99 can be found at page 13, lines 20-34 and elsewhere throughout the specification. Support for dependent claims 100 and 101 can be found at page 10, lines 1-24 and elsewhere throughout the specification. Support for dependent claim 102 can be found at page 3, lines 3-8 and elsewhere throughout the specification. Support for dependent claim 103 can be found at page 18, lines 37-39 and elsewhere throughout the specification. Support for dependent claim 104 can be found at page 23, lines 2-3 and elsewhere throughout the specification. Support for dependent claim 105 can be found in Figure 8 and elsewhere throughout the specification. Support for dependent claim 106 can be found at page 10, lines 37-38 and elsewhere throughout the specification. Support for dependent claims 107 and 108 can be found at page 30, lines 25-29 and elsewhere throughout the specification. Support for claims 109-111 can be found at page 50, line 17-18; page 54, line 26; page 55, lines 1-3; page 57, lines 4-5 and elsewhere throughout the specification. Support for claims 112-117 can be found at page 2, lines 29-34; page 3, lines

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10-15 and throughout the specification. Accordingly, the newly added claims present no new matter.

After careful consideration of the instant Office Action, Applicants respectfully traverse the Examiner's rejections.

Rejection of claims 60-93 under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claims 60-93 under 35 U.S.C. § 112, first paragraph, as not being adequately described because the application allegedly "contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention." Although the Examiner states that the instant application "teaches numerous means for separating the assay locations," she continues to assert that the application does not specifically teach a "non-permanent sealant" separating assay locations and that the application does not "provide any guidance as to what is encompassed by the 'non-permanent sealant' as claimed."

Applicants maintain their arguments as set forth in the response to Office Action filed December 14, 2006. In particular, Applicants respectfully submit that the instant specification at page 10, lines 1-24 provides more than adequate support the term "non-permanent sealant" by exemplifying various materials including, but not limited to, rubber, silicon and gels. However, in order to eliminate this written description rejection so as to simplify the issues should appeal become necessary, Applicants have amended each of the previously pending independent claims (claims 60, 71 and 83) so that the term "non-permanent sealant" is no longer recited. Applicants respectfully submit that each of the currently pending claims is adequately supported by the written description.

In view of the foregoing remarks and amendment, Applicants respectfully request that the Examiner withdraw the rejection under of claims 60-93 under 35 U.S.C. § 112, first paragraph.

Rejection of claims 60-93 under 35 U.S.C. § 103(a)

The Examiner rejects independent claims 60, 71, and 83 under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,232,066 (Felder et al.) in view of U.S. Patent No.

6,023,540 (Walt et al.). In particular, the Examiner asserts that Felder et al. disclose all of the elements of the independent claims except for depressions "being configured to contain a single microsphere." The Examiner then asserts that Walt et al. teach this missing element and that a skilled artisan would be motivated to combine the teachings of these two references because Walt et al. allegedly teach that a single-bead "configuration is important for ensuring that light from each microsphere and reactions occurring on the microsphere are individually detected."

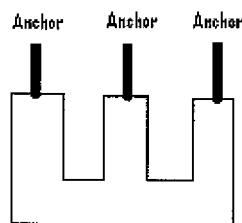
Applicants maintain that claims 60-93 are not obvious in view any of the above-cited references or combinations thereof. Applicants respectfully submit that the limited teaching of Felder et al. regarding the use beads as array substrates does not lend itself to the type of bead usage described in Walt et al. Furthermore, Applicants submit that it is not correct to interpret Felder et al. to teach that an anchor is interchangeable with a bead. As explained below, for at least these reasons, the combination of Felder et al. and Walt et al. does not render claims 60-93 obvious.

As a basis for the above obviousness rejection, the Examiner asserts that Felder et al. disclose a one anchor per dimple relationship at column 6, lines 38-51. The text of this section is reproduced below as follows:

The regions can also be flrther (sic) subdivided such that some or all anchors within a region are physically separated from neighboring anchors by means, e.g., of an indentation or dimple. For example, the number of subdivisions (subregions) in a region can range from about 10 to about 100 or more or less. In one embodiment, a region which is a well of a 1536-well dish can be further subdivided into smaller wells, e.g. about 4 to about 900, preferably about 16 to about 36 wells, thereby forming an array of wells-within-wells. See FIG. 4. Such a dimpled surface reduces the tolerance required for physically placing a single anchor (or group of anchors) into each designated space (locus), and the size of the areas containing anchors is more uniform, thereby facilitating the detection of targets which bind to the probe.

Felder et al. at column 6, lines 38-51.

The Examiner points to Figure 4 of Felder et al. as an illustration of an array of wells-within-wells, wherein anchors are separated from each other by an “indentation or dimple.” Importantly, the Examiner asserts that the sentence “[s]uch a dimpled surface reduces the tolerance required for physically placing a single anchor (or group of anchors) into each designated space (locus), and the size of the areas containing anchors is more uniform, thereby facilitating the detection of targets which bind to the probe” teaches the placement of a single anchor in a single well on a surface. Applicants do not agree that such a teaching is clearly derived from this sentence. Rather, Applicants submit that this sentence actually describes the placement of anchors on the surface between the dimples or indentations. According to this interpretation, the indentations are used to separate anchors from each other as depicted below:



Such an interpretation is consistent with the use of the term “designated space” or “locus” as it appears in the above sentence. It seems to Applicants that if Felder et al. intended that a single anchor be placed within a single indentation or dimple in a substrate, the above sentence would have stated that the anchor be placed into the indentation or dimple.

Nonetheless, even if Applicants were to accept, *arguendo*, that Felder et al. describe the placement of a single anchor within a single indentation as alleged by the Examiner, Applicants cannot agree that the placement of an anchor within the indentation is equivalent to the placement of a bead within the indentation. In other words, Applicants strongly disagree that the term “bead” can be substituted for the term “anchor” and then imported into this single paragraph at column 6, which is alleged to describe a one anchor per indentation arrangement.

Applicants respectfully submit that Felder et al. disclose beads only for use as array substrates. That is, Felder et al. unambiguously describe beads as one of a number of surfaces to which several anchors can be attached. In order to establish this fact, Applicants would like to

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particularly point out the portions of the Felder et al. reference that discuss beads. Felder et al. mention beads, particles or equivalent structures only three times in the entire patent. The first mention of "beads" is at the paragraph bridging columns 4 and 5. Here Felder et al. refer to beads as a potential type of array substrate. In particular, Felder et al. state the following:

Any compatible surface can be used in conjunction with this invention. The surface (usually a solid) can be any of a variety of organic or inorganic materials or combinations thereof, including, merely by way of example, plastics such as polypropylene or polystyrene; ceramic; silicon; (fused) silica, quartz or glass, which can have the thickness of, for example, a glass microscope slide or a glass cover slip; paper, such as filter paper; diazotized cellulose; nitrocellulose filters; nylon membrane; or polyacrylamide gel pad. Substrates that are transparent to light are useful when the method of performing an assay involves optical detection. In a preferred embodiment, the surface is the plastic surface of a multiwell e.g. tissue culture dish, for example a 24-, 96-, 256-, 384, 864- or 1536-well plate (e.g. a modified plate such as a Corning Costar DNA Bind plate). Anchors can be associated, e.g. bound, directly with a surface, or can be associated with one type of surface, e.g. glass, which in turn is placed in contact with a second surface, e.g. within a plastic "well" in a microtiter dish. The shape of the surface is not critical. It can, for example, be a flat surface such as a square, rectangle, or circle; a curved surface; or a three dimensional surface such as a bead, particle, strand, precipitate, tube, sphere; etc.

Felder et al. at column 4, line 63 to column 5, line 18 (emphasis added).

It is important to note that in this paragraph, as well as the other section of the Felder et al. reference where the term "bead" is mentioned, the bead is described as a surface for the association of anchors. It is also relevant to note that Felder et al. state that the shape of the surface is not critical and that many different possibilities for surfaces are described in the above paragraph.

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At this point, it is important to point out that the above paragraph does not describe the attachment of two surfaces via an anchor. Although the above paragraph does disclose that anchors can be associated with a surface, such as a chip or bead, by either binding the anchors directly to that surface, or alternatively, by contacting a first surface having anchors attached thereto with a second surface, for example, placing a chip or bead having anchors attached thereto within a well of a microtiter dish (see column 5, lines 6-18); it is important to recognize that in embodiments where the use of two surfaces is contemplated, there is absolutely no teaching or suggestion of anchors being used to mediate the contact between the first and second surfaces. The lack of such teaching or suggestion is further born out by the definition of the term "anchor" as set forth in the paragraph spanning columns 6 and 7 of the Felder et al. reference. From reading this paragraph, it is clear that, in describing the myriad of substances attachable to anchors, Felder et al. never teach or suggest the attachment of one surface to another via an anchor. Accordingly, Felder et al. disclose that anchors may be attached to a surface, such as a bead, but not to join two surfaces, such as joining a bead to a microtiter well.

Beads that act as a surface for the attachment of anchors, but which themselves are not anchored to wells, is exactly the subject matter described in the only other section of the Felder et al. reference that mentions beads. In particular, this section of the reference discusses of the placement of surfaces having anchors attached thereto into test regions. This discussion, which appears at column 8, lines 39-61, is reproduced as follows:

The anchors do not need to be arranged in a strict or even fixed pattern within each test region. For example, each anchor can be attached to a particle, bead, or the like, which assumes a random position within a test region. The location of each anchor can be determined by the use e.g. of a detectable tag. For example, the linker molecule specific for each type of anchor can be labeled with a different fluorescent, luminescent etc. tag, and the position of a particle comprising a particular linker/anchor pair can be identified by the nature of the signal emanating from the linker, e.g. the excitation or emission spectrum. One skilled in the art can prepare a set of linkers with a variety of such attached tags, each with a distinguishable spectrum. Alternatively, the anchors can be labeled directly. For

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example, each type of anchor can be labeled with a tag which fluoresces with a different spectrum from the tags on other types of anchors. Alternatively, the particles, beads or the like can be different from one another in size or shape. Any of the labeling and detection methods described herein can be employed. For example, fluorescence can be measured by a CCD-based imaging system, by a scanning fluorescence microscope or Fluorescence Activated Cell Sorter (FACS).

Felder et al. at column 8, lines 39-61 (emphasis added).

After reviewing the above disclosure, it becomes clear that this portion of the Felder et al. reference is describing the arrangement of anchors within a test region. The passage states that no regular pattern of anchors is necessary, but rather, can be supplied on beads that are randomly distributed in the test region. The paragraph then goes on to explain that the beads need not be uniform, but rather, can be different from each other in shape or size. As with the previous disclosure regarding beads, this paragraph only describes the use of beads as a substrate for anchors. **It does not equate a single anchor with a single bead.** In fact, nowhere in the Felder et al. reference is a single anchor equated with a single bead. This missing piece of the Examiner's obviousness argument is neither described by Felder et al. nor is it supplied by Walt et al.

As set forth above, Felder et al. only describe beads as one of many substrates that can be used for the attachment of anchors. Thus, even if the Examiner's interpretation of column 6, lines 38-51 as teaching a surface having an anchor within an indentation were correct, at best, a skilled artisan would envision a dimpled bead, not unlike a golf ball, having one or more anchors attached within each dimple. There is absolutely nothing to suggest that a single bead be provided to the dimples. Moreover, there is nothing to suggest that a bead instead of an anchor be provided to the dimples. Finally, there is nothing to suggest that a second bead be attached to the first bead via an anchor within a dimple.

When viewing Felder et al. as a whole, it is clear that the intended use of beads is as a surface for the attachment of anchors is described by at column 8, lines 39-61 of the Felder et al. reference. Column 8 describes the placement of anchors or beads having anchors bound thereto

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within a test region. As described in Applicants' last response, which was filed December 14, 2006, one of ordinary skill in the art would not apply the teachings of Walt et al. so as to adapt the test region disclosed by Felder et al. to a single bead configuration. Such an arrangement would frustrate the purpose of the pattern recognition system described by Felder et al. in the immediately preceding paragraphs (see column 7, line 42 to column 8, line 38). It seems to be only in hindsight that the array systems taught by Walt et al. can be combine with the array systems disclosed by Felder et al. Because Felder et al. do not contemplate the use of beads in a one bead per well relationship, without hindsight, a skilled artisan would not modify the compositions or methods disclosed by Felder et al. by modifying surface indentations to be configured to hold a single microsphere as described by Walt et al. so as to arrive at the claimed invention. As such, Applicants submit that none of claims 60-93 are obvious.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 60-93 under 35 U.S.C. § 103(a).

### CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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